Docket No. 701039-052161 PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Larry I. Benowitz
Serial No.: 09/872,347
Filed: 06/01/2001
Title: METHODS AND COMPOSITIONS FOR PRODUCING A NEUROSALUTARY EFFECT IN A SUBJECT

Examiner: L.I. Riuxiang
Group: 1646

**CERTIFICATE OF MAILING (37 C.F.R. SECTION 1.8(a))**

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the united States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Nicole M. Gignac
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*(Signature of person mailing paper)*

**Commissioner for Patents**
**P.O. Box 1450**
**Alexandria, VA 22313-1450**

## DECLARATION OF LARRY I. BENOWITZ

I, Larry I. Benowitz, declare as follows:

1. I am a inventor of the invention disclosed and presently claimed in the above-identified patent application.

2. I am presently an Associate Professor of Neurosurgery (Neuroscience) at Harvard Medical School. I am also the Director of the Laboratory for Neuroscience at Children's Hospital (Boston). A copy of my *curriculum vitae* is attached as Appendix A.

3. Under my direction and control polymeric beads releasing oncomodulin (OM) or dibutyrl-cAMP (dBcAMP) were tested to determine their effect on stimulating mature rat retinal ganglion cells (RGCs) to regenerate their

axons through an injured optic nerve crush *in vivo* (n = 2-4 per group). The model used is as described in our recent publications (e.g., Yin Y, Cui Q, Li Y, Irwin N, Fischer D, Harvey AR and Benowitz LI. (2003) J. Neurosci, 23: 2284-2293).

4. The attached figure (Appendix B) shows the number of RGC axons regenerating either 0.5 (light bars) or 1.0 mm distal to an injury site in the optic nerve. Negative controls include optic nerve crush (NC) with only a minimal injury to the retina, or similar surgery but injection of blank beads. The positive control is the amount of regeneration obtained by activating macrophages in the eye with Zymosan. **p , 0.01; ***p , 0.001 compared to either negative control. As shown in the attached figure, dBcAMP alone had no effect on growth; while OM plus dBcAMP caused many RGCs to regenerate their axons through the optic nerve.

5. As noted above, the model used in this work is standard in the field. Our publication using this, which cites prior references in the field, is attached as Appendix C.

6. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application and any patents issuing thereon.

Date: May 29, 2003

Larry Benowitz

Larry I. Benowitz, PhD